

**REMARKS**

In this Amendment, Applicant has amended Claim 1 to correct a clerical error. The support of the amendment can be found on page 2, line 18 of the specification. It is respectfully submitted that no new matter has been introduced by the amended claim. All claims are now present for examination and favorable reconsideration is respectfully requested in view of the preceding amendments and the following comments.

**REJECTIONS UNDER 35 U.S.C. § 103:**

Claims 1 – 6 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Vadenmersch et al. (US2004/0235664), hereinafter US'664, in view of Matrosovich et al. (US 6,232,494), hereinafter US'494, further in view of Smith (US 5,087,740), hereinafter US'740.

Applicant traverses the rejection and respectfully submits that the embodiments of present-claimed invention are not obvious over US'664 in view of US'494 and US'740. More specifically, the inventions defined in the claims are significantly different from the disclosures of these references. There is no motivation or suggestion in the prior art that would teach the combination of these references. Even if they are combined, the combination would not teach or suggest the amended claims as presented.

The present invention defines a process to purify Glyphosate solutions (N-phosphonomethylglycine) obtained from the synthesis of Glyphosate by oxidation of N-phosphonomethyliminodiacetic acid and containing formaldehyde and formic acid as main impurities, comprising the steps of: providing an initial solution of Glyphosate with a Glyphosate concentration ranging between 0.1% and 3% w/v, a formaldehyde concentration ranging between 0.5% and 1% w/v, and a formic acid concentration ranging between 0.1% and 0.6% w/v; adjusting the pH of the said initial Glyphosate solution to a value ranging between 2.5 and 3.5 with a base selected from alkylamine,

ammonium hydroxide, sodium, or potassium hydroxide; submitting said solution to nanofiltration at a temperature ranging between 10 °C and 35 °C and a pressure ranging between 25 and 35 Kg/cm<sup>2</sup>; carrying out said nanofiltration through at least one nanofiltration membrane; recovering the concentrated Glyphosate solution containing more than 97% of Glyphosate from the initial solution with a Glyphosate concentration of approximately 8%; and discarding the permeate solution containing between 50% and 95% of formaldehyde and formic acid present in said initial solution. According to this process, a concentrated solution of Glyphosate with a recovery of more than 97% of Glyphosate and concentration of impurities, formic acid and formaldehyde of up to 95% is obtained from an original solution of up to 8% by a nanofiltration operation.

US'740 relates to a method for obtaining purified N-phosphonoethylglycine (Glyphosate) from aqueous solutions containing N-phosphonomethylglycine and other organic impurities. The method disclosed in US'740 comprises the step of causing the aqueous solution containing N-phosphonomethylglycine to circulate through a column containing a weak basic ionic interchange resin in order to retain organic impurities more acid than N-phosphonomethylglycine. Subsequently, the effluent of that column is made to circulate through a second column also containing a weakly basic ionic interchange resin and retaining the N-phosphonomethylglycine, which is finally recovered from said second column by its elution with a base and a strong mineral acid. All the description of US'740 is aimed only at explaining a process for separating Glyphosate from its impurities by using weakly basic ionic interchange resins. The prior art description at the beginning of the description of said reference does not contain any suggestion of or reference to any alternative process for separating Glyphosate by other techniques different from the one claimed in US'740.

Furthermore, US'740 does not disclose that the method claimed might involve any problem or difficulty of technical nature, for which reason it cannot be discerned nor understood how a person skilled in the art might be prompted from the information contained in patent US'740 to obviously conclude the application of the nanofiltration technology for separating Glyphosate from its organic impurities (formic acid and

formaldehyde) if US'740 makes reference only to an optimal separation technique using ionic interchange resins, an operation that not only is not a filtration but that is a process involving reversible chemical reactions, which are completely absent in a nanofiltration operation.

Moreover, in the examples included in US'740 (see column 6), there are Glyphosate aqueous solutions undergoing ionic interchange with resins and which are made up by diverse both organic and inorganic impurities. Hence, the solutions assayed in said reference are neither identical nor equivalent to the Glyphosate aqueous solutions that are nanofiltrated in present application and which contain only organic impurities represented by formic acid and formaldehyde. Therefore, a person skilled in the art would have no reason at all to imagine alternative solutions to the one posed in US'740.

US'494 discloses a method for preparing N-phosphonomethylglycine, its salts and esters, comprising essentially reacting with oxygen a N-substituted N-phosphonomethylglycine in the presence of a polymer-supported noble metal catalyst. As it can be noticed, for instance in claims 1 and 15 of US'494, the starting compound in this method is an N-substituted N-phosphonomethylglycine of general formula V that does neither encompass nor include N-phosphonomethyliminodiacetic acid, which is the starting compound originating, by oxidation, the Glyphosate aqueous solutions containing formic acid and formaldehyde and which are nanofiltrated in the process of instant application.

Particularly, general formula V of claim 1 of US'494 excludes specifically N-phosphonomethyliminodiacetic acid, by pointing out that groups R1 and R2 stand for the “substituted hydrocarbyl other than -CO<sub>2</sub>R15” group. In other words, the compounds of formula V of claim 1 of US'494 never do possess two carboxy (-COOH) groups, and consequently the oxidation products of the compounds of formula V will always be different from the oxidation products of N-phosphonomethyliminodiacetic acid, which contains two carboxy groups. Therefore, the products of reacting with oxygen N-substituted N-phosphonomethylglycine, in accordance with the method of patent US'494,

are different from the reaction products obtained from N-phosphonomethyliminodiacetic acid (PMIDA) and which are part of the starting aqueous solutions of the process disclosed in instant application (Glyphosate-formic acid-formaldehyde).

In addition, US'494 discloses, beginning from its claim 31, that the mixing of the oxidation products of the main reaction (foreseen in claim 1) is separated in two

Glyphosate, its salts and esters, and a second liquid fraction called "residual mixture". Separating the two fractions is performed, for instance, by crystallizing Glyphosate, its salts and esters, as indicated in column 18, lines 44 to 46 of the description of US'494. The "residual mixture", as indicated in claim 36, may be divided in two currents: a recycling current, which returns to the reactor from which the main oxidation reaction is produced, and a waste out current. Separating the "residual mixture" into these two currents is achieved by contacting the "residual mixture" with a membrane, by forming a retentate current containing Glyphosate, its salts or esters, and the not reacted N-substituted N-phosphonomethylglycine, and a waste out (permeate) current containing the impurities passing through the membrane.

As indicated in lines 14 and 15 of column 25 of US'494, the separation of the "residual mixture" by a membrane is described (only) in Example 30 of the reference. In said Example 30 is shown the application of several membranes of nanofiltration for (trying to) remove selectively the bisulfate ions of a simulated solution containing Glyphosate, N-methyl-Glyphosate and dihydrophosphate (see lines 21 to 23 of column 30). This simulated pH 1.4 solution is representative of the solution obtained after the obtainment of N-substituted Glyphosate by phosphonomethylation catalyzed by H<sub>2</sub>SO<sub>4</sub> and subsequent oxidation. The results of these experiences are included in Table 24 (see column 51). The results on Table 24 indicate essentially that only two of the assayed membranes (called SelRO MPF-34/36) are relatively useful for the ends proposed in the assay. In fact, the "36" membrane, though selective for removing the bisulfate ions (selectivity 4.87), is not selective for retaining the phosphate ions (selectivity 1.03), as it does not either substantially retain Glyphosate (since its efficiency is 0.8). The same

happens with the "34" membrane, which, though effective for retaining Glyphosate, is not selective for the phosphate ions (selectivity 1.49). The two membranes do not substantially retain the N-methyl-Glyphosate, even though its molecular weight is higher than that of Glyphosate. Even though, for the reasons given, the results shown in Table 24 look incomplete to justify the industrial level application of nanofiltration in a system as the one disclosed in Example 30, what is certain is these results could allow a person skilled in the art to formulate a priori the following considerations:

- The membranes of the SelRO type may be useful for separating selectively inorganic ions: even inorganic ions of a similar molecular weight, such as the sulfate and phosphate ions.
- In US'494 there are found no experimental data teaching or suggesting that the SelRO type membranes or any other type of membranes be useful for selectively separating compounds of organic nature; even less than that are there found any suggestions or teachings permitting to infer or suppose that such membranes be useful for separating and purifying Glyphosate from its organic impurities resulting from the oxidation of PMIDA.

Therefore, having in view the information disclosed in the description and examples of US'494 concerning the application of nanofiltration and not knowing the contents of the present application, Applicant respectfully submits that the person skilled in the art would only be induced to think how to optimize the experiments shown in Example 30 and particularly how to remove selectively the bisulfate ions of a solution containing Glyphosate, N-methyl-Glyphosate and dihydrogenphosphate ions. Since the nanofiltration technique used in US'494 does not focus on a Glyphosate purification process and even less on the purification of Glyphosate in an aqueous solution coming from the oxidation of PMIDA, it is not discernable how the person skilled in the art might be induced obviously to think, prompted by the teachings of US'494, that the nanofiltration might be appropriate for separating Glyphosate from its organic impurities constituted by formic acid and formaldehyde.

US'664 relates to a process for recovering Glyphosate from Glyphosate-containing aqueous solutions, ammonium halides, alkali metal or alkaline-earth metal halides and, optionally, dissolved organic impurities. Said process comprises essentially subjecting a pH 2-8 Glyphosate-containing aqueous solution, ammonium halides, alkali metal and alkaline-earth metal halides and, optionally, dissolved organic impurities, to a nanofiltration operation with the purpose of obtaining a retentate enriched in Glyphosate and impoverished in halides and an permeate impoverished in Glyphosate and enriched in halides. The process described and claimed in US'664, as reported in its paragraphs [0005], [0006] and [0020], was developed for recovering the Glyphosate obtained from the chemical reaction between a hexahydrotriazine (see formulas II and II-a of the reference) and a triacylphosphite and subsequent acid hydrolysis of the product obtained. After the separation of Glyphosate by crystallization at pH 0.5-2, the mother liquors are subjected to a nanofiltration operation.

Nevertheless, US'664 makes it clear, in its paragraph [0005], that the mother liquors have a composition completely different than the mother liquor obtained in the oxidation of N-phosphonomethyliminodiacetic acid (PMIDA), since apart from Glyphosate, said mother liquors contain small quantities of aminomethylphosphonic acid, glycine, bis(phosphonomethyl)glycine and large quantities of chloride salts. In its paragraph [0019], US'664 specifies that the quantity of halides present in the mother liquors is of at least 8 %, particularly of at least 10 % and particularly preferably of at least 12 %. Therefore, the aqueous solution that is subjected to nanofiltration in the process of US'664 has a chemical composition that is completely different from the chemical composition of the aqueous solution subjected to nanofiltration in the method of instant application (Glyphosate-formic acid-formaldehyde).

Particularly, in the Tables included in examples 1 and 2 of US'664, there are indicated the compositions in percentages of the solution that retains the nanofiltration membrane (retentate) and the solution that passes through said membrane (permeate). As it can be learned from the information supplied by said tables, the nanofiltration process of US'664 is not either a Glyphosate purification process, as the method of instant

application is, while the solution retained (retentate) by the nanofiltration membrane keeps a high concentration of salts (NaCl/NH<sub>4</sub>Cl) and of the remaining impurities presenting the starting solution or mother liquor (aminomethylphosphonic acid, glycine and bis(phosphonomethyl)glycine). Hence, it is not discernable how the person skilled in the art might deduce as obvious from the information supplied in application US'664 the successful application of the nanofiltration to a system so different as is an aqueous solution containing Glyphosate, formic acid and formaldehyde.

Moreover, it is respectfully submitted that the person skilled in the art, when faced with the technical problem of the purification of Glyphosate from Glyphosate aqueous solutions containing formic acid and formaldehyde as main organic impurities, **would not have used nanofiltration as separation and purification method, since US'664 does strongly suggest that the nanofiltration process is not appropriate for separating and purifying Glyphosate from a solution containing also formic acid and formaldehyde.** In fact, focusing on the experimental results included in Examples 1 and 2 (Tables 1 and 2) of US'664, it can be noticed that the **Desal 5 DK membrane** used for nanofiltrating the compositions in both examples and which, according to the manufacturer, do have a cutting limit situated between 150 and 300 g/mol, **is not useful for removing the glycine from the retentate aqueous solution (which contains Glyphosate).** In other words, **the only impurity having organic nature (Glycine), whose solutions were assayed in Examples 1 and 2 of application US'664 could not be significantly separated by nanofiltration in a Glyphosate-containing solution,** even though the molecular weight of the glycine, of 75 g/mol, is well below the membrane cutting limit, which is of 150-300 g/mol. Therefore, **such information would have induced the person skilled in the art into thinking that nanofiltration is not selective for separating formic acid and formaldehyde from a solution containing Glyphosate and the two impurities of organic nature.** It is even less likely that such information might have induced the person skilled in the art into thinking that a **Glyphosate aqueous solution containing formic acid and formaldehyde could have been purified by nanofiltration.** **Therefore, the process of present application is not obvious over**

**the teachings and suggestions disclosed in US'664 in combination with US'494 and US'740.**

As for the contents of patent IT 01281094, mentioned in paragraph 2 of the US'664, Applicant must point out that said patent relates to the nanofiltration of solutions containing Glyphosate and formaldehyde and resulting from the catalytic oxidation of N-phosphonomethyliminodiacetic acid (PMIDA) with air or oxygen. Nevertheless, patent IT '094 does not describe, nor exemplify or claim, the nanofiltration of aqueous solutions of Glyphosate containing formic acid, as one of the main products resulting from the oxidation reaction of PMIDA, along with formaldehyde, so as is exemplified and claimed in the present application. Furthermore, patent IT'094 only exemplifies and describes the nanofiltration of Glyphosate-formaldehyde solutions in which Glyphosate is in the form of a free acid (examples 1-3 of patent IT) or in the form of salt (examples 4 and 5 of patent IT), but never in the form of acid partially neutralized to pH 2.5-3.5, as in the process exemplified and claimed in the Vigil et al application. For this reason, Applicant respectfully submits that the nanofiltrating to controlled pH, comprised between 2.5 and 3.5, and the presence of formic acid in the solutions that are nanofiltrated in the method of the present invention, is significantly different from and non-obvious over IT'094.

It is respectfully submitted that IT'094 consists in at least partially stripping the formaldehyde present in a Glyphosate coming from a catalytic oxidation of PMIDA. Separating formaldehyde is done by inverse osmosis or by nanofiltrating an aqueous solution containing Glyphosate, as free acid or in salting form. According to IT'094, this operation of separating by using a membrane is carried out to avoid the distillation stage of the formaldehyde (see Esempio B: prova de controllo) resulting in a loss of yield (87%) in the recovery of Glyphosate because of the secondary reaction of the formaldehyde with the Glyphosate. Hence, in Example 1 of patent IT'094, the formaldehyde is partially removed from a solution of Glyphosate, as free acid, and formaldehyde, by using an inverse osmosis membrane, thereby obtaining a retentate in which about 21 % of the formaldehyde present in the original solution has been

**eliminated.** In the following Examples 2 and 3 the same technique of Example 1 is repeated, thereby obtaining **retentate solutions in which 26 % and 18 %, respectively, of the original formaldehyde have been eliminated.** In Example 4 of patent IT'094, there is described the separation of formaldehyde from a Glyphosate solution, neutralized with a molar excess of isopropylamine by inverse osmosis. In said Example there are carried out two successive operations of inverse osmosis by using membrane, thereby obtaining at the end a retentate solution from which about 75 % of the formaldehyde has been eliminated. Nevertheless, **the recovery of Glyphosate has dropped to about 92 %.** Finally, in Example 5 of patent IT'094 the technique employed in Example 4 is repeated, but by using a nanofiltration membrane. At the end, what is obtained is a **retentate solution containing** about 21 % of the formaldehyde of the original starting solution with **a recovery of the salt of the Glyphosate of about 92 %.**

In view of the experimental results of Examples 1 to 5 of patent IT '094, Applicant respectfully submits that the person skilled in the art could easily reach the following conclusions:

- a) **Inverse osmosis is not very useful for removing formaldehyde from an aqueous solution of Glyphosate, as free acid or in salting form,** because the removal degree of formaldehyde is very low (between 18 % and 26 %, according to the Examples of patent IT) when an operation is performed in one stage, while when it is done in two stages, even though up to 75 % of the formaldehyde is removed, the recovery of Glyphosate drops to values near to those obtained by the prior art technology (87 %).
- b) **Nanofiltration, performed in one or more consecutive stages, does not significantly improve the experimental results obtained with inverse osmosis membranes in regard to formaldehyde removal (removal near to 80 %), neither does it improve the recovery of the Glyphosate salt, which is of about 92 %.**
- c) **Neither inverse osmosis nor nanofiltration are operations that are useful for purifying formaldehyde-containing Glyphosate aqueous**

**solutions, since by increasing the formaldehyde removal to levels that exceed 80 %, the percentage of recovery of Glyphosate, or of Glyphosate salts, would proportionally drop to values that are unacceptable, lower than 90 %.**

In conclusion, patent IT'094 does neither teach nor suggest that the **nanofiltration operation is useful for purifying formaldehyde-containing Glyphosate solutions**. Within the context of the technical field that is being perused, by purification is understood the operation that turns out to be effective for recovering the active component with a recovery percentage higher than 95 % and a purity degree of more than 90 %. For this reason, Applicant respectfully submits that **patent IT'094 would actually prompt the person skilled in the art to disregard the application of nanofiltration as a purification technique of Glyphosate aqueous solutions coming from the oxidation of PMIDA**. Therefore, **the achievement of the present application is evident**: against the teachings and suggestions of the prior art perused, contemplated on its own or in combination, **the process claimed in the present application has solved, in a simple, both unexpected and surprising manner, a technical problem underlying in prior art.**

In fact, as it has been shown above, **the purification of aqueous solutions of Glyphosate and formaldehyde that do also contain formic acid, by nanofiltrating them under controlled pH conditions, is not only a method that is novel, but also clearly inventive, inasmuch as neither its realization nor its results might have been deduced through self-evidence by a person skilled in the art.**

Applicant respectfully submits that no hindsight gained from the present application should be used in analyzing the obviousness of the combination of relevant references.

In summary, US'740, contemplated on its own or in combination with the other citations, does not defeat the inventiveness of the process claimed in instant application,

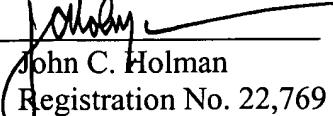
inasmuch as it relates to a process of ionic interchange by resins, which has no connection at all with the nanofiltration process claimed in instant application. US'494 does not defeat the inventiveness of the process claimed in instant application, because the solutions that are being nanofiltrated in said patent have a composition that is completely different to the solutions nanofiltrated in instant application. Furthermore, in the citation there are no teachings or suggestion that permit to infer that the nanofiltration membranes might be useful for purifying Glyphosate solutions containing impurities of organic nature. US'664 does not defeat either the inventiveness of the process claimed in instant application, since its teachings and suggestions point in a direction that is opposite to the experimental results exemplified in instant application. In fact, in this reference, it is experimentally demonstrated that the use of a nanofiltration membrane is not useful for removing an organic impurity of low molecular weight, such as Glycine, from an aqueous solution containing Glysophate. For this reason, this reference alone or combined with the teachings of US'494, does neither disclose nor suggest in an obvious manner the application of a nanofiltration operation for satisfactorily purifying Glyphosate solutions resulting from the oxidation of PMIDA. Thus, the newly presented claims are not obvious US'664 in view of US'494 and US'740. The rejection under 35 U.S.C. § 103 has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 103 is respectfully requested.

Having overcome all outstanding grounds of rejection, the application is now in condition for allowance, and prompt action toward that end is respectfully solicited.

Respectfully submitted,

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